2-X8 (HCO_3^-) ion-exchange resin. The neutralized solutions were filtered free of resin, the resin was washed with a small amount of methanol, and the combined filtrate and wash were concentrated *in vacuo* (35° bath) to a residual solid. The residue was dissolved in CH_3OH (50 ml) and diluted with ether (75 ml) and hexane (100 ml). The solution was seeded and stored at 5° for 16 hr to give the product as a crystalline solid (3.4 g, 0.0123 mole, 24.6%), mp 170–171.5°. Continued storage afforded a second crop (1.7 g, 34% total). The material was homogeneous by tlc (silica gel–benzene–*n*-butylamine–water, 15:5:1). An analytical sample was prepared by recrystallization from a methanol–ether mixture containing a trace of hexane: mp 172–173°, $[\alpha]^{25}D$ +178.1° (*c* 1.0, CH_3OH), λ_{max}^{EtOH} 290 mμ (ε 6500), λ_{min}^{EtOH} 244 mμ (ε 845).

Anal. Calcd for $C_{10}H_{13}FN_2O_6$: C, 43.48; H, 4.75; N, 10.14; F, 6.88. Found: C, 43.24; H, 4.76; N, 9.88; F, 7.09.

A coupling run on the same scale as above (5 days) without the addition of molecular sieves yielded only 2.4 g (17%) of **3**.

1-β-D-Arabinofuranosyl-5-fluorocytosine (1).—A solution of **3** (2.76 g, 0.01 mole) in a 5% solution of anhydrous NH_3 in CH_3OH (200 ml) was sealed in a glass-lined bomb which was heated in an oil bath at ~125° for 16 hr. The bomb was cooled and opened and the contents was evaporated to dryness *in vacuo*. The residue was triturated with a small amount of CH_3OH, filtered, washed, and dried *in vacuo* to give 1 (2.3 g, 88%), mp 234–235° dec. The compound moved as a single spot on tlc (silica gel–benzene–*n*-butylamine–water, 15:5:1) and was free of starting material. The material was recrystallized once from a hot CH_3OH–H_2O mixture to give pure 1, mp 230–232° dec, $[\alpha]^{25.5}D$ +165.2° (*c* 0.2, H_2O) [lit.[3] mp 237–238°, $[\alpha]^{23}D$ +163 ±2° (*c* 0.18, H_2O)]. The ultraviolet and infrared spectra were identical with those of a sample prepared from **2** by the method of Fox, *et al.*[2]

1-β-D-Arabinofuranosyl-5-fluorouracil (2).—The 4-alkoxy derivative **3** (0.6 g, 2.07 × 10^{-3} mole) was dissolved in 1 *N* HCl in methanol (20 ml), and the tightly stoppered solution was stored for 72 hr at ambient temperature. The solution was evaporated to dryness *in vacuo* and the residue was dissolved in a minimum of absolute EtOH, seeded, and stored at ~5° to give **2** (0.35 g, 65%) in two crops: mp 187–189, 184–185°. The combined crops were recrystallized once from hot absolute EtOH to give pure **2**, mp 186–188°, $[\alpha]^{24.5}D$ +116.7° (*c* 0.2, H_2O) [lit.[3] mp 187–188°, $[\alpha]^{24}D$ +128° (*c* 0.21, H_2O)[4]. The ultraviolet and infrared spectra were in good agreement with those of an authentic sample.

Acknowledgment.—The authors express their appreciation to Hoffmann-LaRoche, Inc., for a generous gift of 5-fluorouracil for use in this study. We wish to thank Mr. H. I. Zuak of the Riker Analytical Department for obtaining the spectral data.

Terpene Compounds as Drugs. III. Terpenylketoximes

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Received March 20, 1967

The report[1] that some oximes of aliphatic ketones are endowed with interesting hypnotic and anticonvulsant properties and our interest in the terpene field have led us to synthesize the oximes of geranylacetone, nerylacetone, and farnesylacetone and to study their pharmacological properties. However, none of the three compounds displayed hypnotic and anticonvulsant activity of any interest. By contrast, geranylacetone oxime and nerylacetone oxime revealed a marked and unexpected hyperglycemic activity in rats and rabbits.

Experimental Section

Geranylacetone Oxime.—Geranylacetone[2] (4.6 g, 0.0237 mole), hydroxylamine hydrochloride (2.47 g, 0.0355 mole), and $NaHCO_3$ (2.98 g, 0.0355 mole) were poured into 10 ml of water, and the mixture was stirred for 24 hr at room temperature. An emulsion formed which was then extracted with ether, the ethereal solution was washed with water and dried (Na_2SO_4), and the solvent was removed. The residue was distilled *in vacuo* to yield a colorless oil (4.1 g, 83%), bp 107–108° (0.05 mm), $n^{20}D$ 1.4897, lit.[3] $n^{20}D$ 1.4894.

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.58; H, 11.07; N, 6.69. Found: C, 74.74; H, 11.06; N, 6.51.

Nerylacetone oxime was similarly prepared from nerylacetone[2] with an 84% yield, bp 112–114° (0.12 mm), $n^{20}D$ 1.4890.

Anal. Calcd for $C_{13}H_{23}NO$: C, 74.58; H, 11.07; N, 6.69. Found: C, 74.55; H, 11.18; N, 6.49.

Farnesylacetone oxime was derived from farnesylacetone[2] in an 81% yield, bp 142–143° (0.07 mm), $n^{20}D$ 1.4974.

Anal. Calcd for $C_{18}H_{31}NO$: C, 77.92; H, 11.26; N, 5.05. Found: C, 77.75; H, 11.05; N, 4.90.

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Formation of 4-Amino-3,5-di(3-indolylmethyl)-*s*-triazole from Indole-3-acetonitrile and Hydrazine

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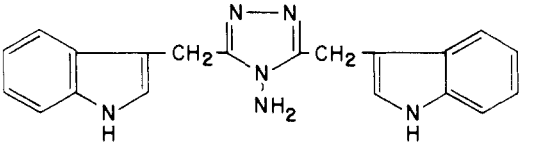
Received May 17, 1967

During investigations of the chemistry of indolic compounds and possible routes to tryptamines, indole-3-acetonitrile was treated with anhydrous hydrazine. Analytical data obtained together with consideration of reactions reported in the Experimental Section led to the structural assignment as 4-amino-



3,5-di(3-indolylmethyl)-*s*-triazole for the compound obtained.

Experimental Section

Mass spectroscopy was performed by the Morgan Schaffer Corp., Montreal 26, Quebec, Canada. Nmr spectra was done by Nuclear Magnetic Resonance Specialties, Inc., New Kensington, Pa.

Indole-3-acetonitrile (5.0 g, 0.032 mole) was refluxed with 25.0 ml of anhydrous hydrazine for 18 hr. Most of the hydrazine was removed under vacuum and the residual solution was poured into water resulting in the precipitation of 6.1 g (56% yield) of light yellow product, mp 224–226. Three crystallizations from ethanol–water gave a cream-colored compound, mp 227–228° (cor).

Anal. Calcd for $C_{20}H_{18}N_6$: C, 70.15; H, 5.30; N, 24.55. Found: C, 70.42; H, 5.52; N, 24.22.

Chromatography on thin layer silica on glass in 9:1 $CHCl_3$–CH_3OH produced one spot at R_f 0.1 giving a positive xanthydrol reaction for indoles, negative ninhydrin reaction, and weak fluorescence under uv light. The compound was insoluble in water, but soluble in dilute HCl. Mass spectroscopic analysis gave 342 as the parent peak and therefore molecular weight. The infrared absorption spectrum (KBr) showed the presence of the N–H stretching band at 2.95 μ. The uv spectrum (in

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ethanol) gave a peak of 280 mμ typical for indoles and it did not change after acidification. The nmr spectrum contained five peaks and was interpreted after integration as representative of eight aromatic hydrogens (τ 1.0–3.0), two pyrrole N–*H*, two N–N*H*$_2$, four C*H*$_2$, and two indole-2 hydrogens.

2-Hydrazino-8-quinolinol and Derivatives[1]

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Received March 31, 1967

Hydrazones of carbonyl compounds and 2-hydrazino- and 2-(1-methylhydrazino)-8-quinolinols were prepared for antitumor tests. Those hydrazones from formyl-8-quinolinols might be of further interest as bifunctional chelating agents.[2,3]

Experimental Section[4]

2,8-Quinolinediol[5] was tosylated and chlorinated with PCl_5–$POCl_3$ in agreement with the literature,[6] although final hydrolysis with alkali to 2-chloro-8-quinolinol gave a product of substantially higher melting point (83–84°) than reported.

2-Hydrazino-8-quinolinol.—2-Chloro-8-quinolinol (5 g) was refluxed in 20 ml of 40% hydrazine for 4 hr. Solvent was removed under vacuum and 15 ml of water was added to precipitate the product. Recrystallization from 95% ethanol yielded a tan solid, mp 177–178° (81% yield).

Anal. Calcd for $C_9H_9N_3O$: C, 61.70; H, 5.17; N, 23.97. Found: C, 61.87; H, 5.09; N, 23.84.

Although reasonably stable as the solid, the hydrazine in solution decomposed in a few hours. The ultraviolet spectra in various solvents showed λ_{max} [mμ (log ε)]: EtOH, 245 (4.27), 263 (4.46), 280 s (4.04); 0.1 *N* HCl, 240 (4.12), 264 (4.40), 304 (3.87), 340 s (3.52); 0.1 *N* NaOH, 252 (4.36), 274 s (4.02), 330 (3.46), 356 s (3.41). The infrared spectra (KBr) showed bands at 3345, 3330, 1520, 1240, 820, and 738 cm^{-1} (strongest bands).

2-(1-Methylhydrazino)-8-quinolinol.—2-Chloro-8-quinolinol (1 g) and 0.39 g of methylhydrazine in 1-propanol as solvent were refluxed 24 hr. Evaporation of solvent, addition of 50 ml of water, and neutralization with K_2CO_3 precipitated the product, mp 106° after recrystallization from ligroin (80% yield). The ultraviolet spectra showed λ_{max} [mμ (log ε)]: EtOH, 250 s (4.27), 269 (4.52), 351 (3.56); 0.1 *N* HCl, 244 (4.23), 269 (4.48), 312 (3.48), 351 (3.71); 0.1 *N* NaOH, 279 (4.56), 318 s (3.18), 360 s (3.69).

Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.80; N, 22.19. Found: C, 63.49; H, 5.70; N, 22.12.

Preparation of Hydrazones.—Equimolar amounts of the hydrazine and aldehyde or ketone were refluxed in ethanol for 0.5–5 hr to precipitate the hydrazones, generally yellow solids. Aldehydes reacted more quickly than ketones. Filtration of the products and recrystallization, generally from benzene, gave 80–95% yields of the compounds listed in Table I. Absorption spectra of some of these hydrazones were determined as follows for the carbonyl compound: λ_{max}^{EtOH} [mμ (log ε)]: 7-formyl-8-quinolinol, 249 (4.33), 290 s (4.27), 306 (4.40), 381 (4.37), 436 (3.69); 5-acetyl-8-quinolinol, 243 (4.51), 289 (4.46), 359 (4.12); 2-formylpyridine, 238 (4.19), 264 (4.17), 274 s (4.12), 318 s (4.34), 352 (4.45), 439 s (3.30).

TABLE I

HYDRAZONES FROM 2-HYDRAZINO-8-QUINOLINOL AND CARBONYL COMPOUNDS

Carbonyl compd	Mp, °C[a]	Formula	% carbon Calcd	% carbon Found	% hydrogen Calcd	% hydrogen Found	% nitrogen Calcd	% nitrogen Found
5-Acetyl-8-quinolinol	218	$C_{22}H_{16}N_4O_2$	69.75	69.60	4.68	4.75	16.26	16.10
5-Acetyl-2-methyl-8-quinolinol	207	$C_{21}H_{18}N_4O_2$	70.38	70.45	5.06	5.20	15.63	15.83
4-Formyl-8-quinolinol	292	$C_{19}H_{14}N_4O_2$	69.93	69.24	4.32	4.40	15.94	16.15
5-Formyl-2-methyl-8-quinolinol	233	$C_{20}H_{16}N_4O_2$	69.75	69.57	4.68	4.84	16.26	16.11
7-Formyl-8-quinolinol	289	$C_{19}H_{14}N_4O_2$	69.93	70.08	4.32	4.52	15.94	16.08
7-Formyl-2-methyl-8-quinolinol	277	$C_{20}H_{16}N_4O_2$	69.75	69.53	4.68	4.83	16.26	16.14
7-Formyl-5-methyl-8-quinolinol	268	$C_{20}H_{16}N_4O_2$	69.75	69.92	4.68	4.91	16.26	16.09
Salicylaldehyde	239	$C_{16}H_{13}N_3O_2$	68.81	68.43	4.69	4.75	15.04	14.77
p-Dimethylaminobenzaldehyde	239	$C_{18}H_{18}N_4O$	70.58	70.30	5.92	6.14	18.28	17.98
Pentafluorobenzaldehyde	254	$C_{16}H_{18}F_5N_3O$	54.40	54.23	2.28	2.17	11.89	11.76
Phthalaldehydic acid	225	$C_{17}H_{13}N_3O_3$	66.45	66.64	4.26	4.46	13.67	13.47
2-Formylpyridine	214	$C_{15}H_{12}N_4O$	68.17	68.19	4.57	4.66	21.19	21.32
3-Formylpyridinium methiodide	231	$C_{16}H_{15}IN_4O$					13.79	14.60
4-Antipyrinecarboxaldehyde	248	$C_{21}H_{19}N_5O$	67.55	67.33	5.13	5.17	18.74	18.53
Salicylaldehyde[b]	206	$C_{17}H_{15}N_3O_2$	69.62	69.90	5.15	5.30	14.32	13.96

[a] Upper end of a 1–2° range. [b] Hydrazone of 2-(1-methylhydrazino)-8-quinolinol.

(1) This work was supported by a grant from the U. S. Public Health Service (CA 07403).

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3-Aminospirohydantoins

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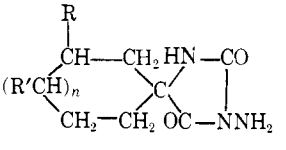
Received May 10, 1967

Some 3-amino-5,5-disubstituted hydantoins have a pronounced diuretic effect.[2] Such hydantoins have been prepared from the dihydrazide of α-substituted glycine-*N*-carboxylic acids,[2–5] and



I, $n = 0$; R = H
II, $n = 1$; R, R′ = H
III, $n = 2$; R, R′ = H
IV, $n = 3$; R, R′ = H
V, $n = 1$; R = CH_3; R′ = H
VI, $n = 1$; R = H; R′ = CH_3

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